Dicer-microRNA-Myc circuit promotes transcription of hundreds of long noncoding RNAs.

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Public Summary:
Long noncoding RNAs (lncRNAs) are a newly recognized class of genes that can control cell fates. It was always assumed that lncRNAs are produced in the same manner as regular protein coding genes. This work revealed that a specialized production system for lncRNAs. This allows many lncRNAs to be produced or turn off together. Many lncRNAs important for embryonic stem cell biology are under this control system, and lncRNA production is also systematically affected in many human cancers.

Scientific Abstract:
Long noncoding RNAs (lncRNAs) are important regulators of cell fate, yet little is known about mechanisms controlling lncRNA expression. Here we show that transcription is quantitatively different for lncRNAs and mRNAs-as revealed by deficiency of Dicer (Dcr), a key RNase that generates microRNAs (miRNAs). Dcr loss in mouse embryonic stem cells led unexpectedly to decreased levels of hundreds of lncRNAs. The canonical Dgcr8-Dcr-miRNA pathway is required for robust lncRNA transcriptional initiation and elongation. Computational and genetic epistasis analyses demonstrated that Dcr activation of the oncogenic transcription factor cMyc is partly responsible for lncRNA expression. A quantitative metric of mRNA-lncRNA decoupling revealed that Dcr and cMyc differentially regulate lncRNAs versus mRNAs in diverse cell types and in vivo. Thus, numerous lncRNAs may be modulated as a class in development and disease, notably where Dcr and cMyc act.